REMARKS

FORMAL MATTERS:

Claims 26, 28-29, 54-60, 66-68, 70-75, and 80-86 are pending and currently under examination.

Claims 26, 28-29, 54-60, 66-68, 70-75 and 80-86 were rejected.

No new matter is added.

REJECTION UNDER 35 U.S.C. §103(a)

Claims 26, 28-29, 54-60, 66-68, 70-75, and 80-86 were rejected under 35 U.S.C. §103(a) as allegedly being obvious over Manning et al. (WO 97/38698) ("**Manning**") in view of Tamada et al. (See "The development of polyanhydrides for drug delivery applications") ("**Tamada**") and further in view of Husmann et al. (See "Hearing Research, Round window administration of gentamicin; a new method for the study of ototoxicity of cochlear hair cells") ("**Husmann**") Applicants respectfully traverse the rejection as discussed below.

The Patent Office bears the burden of establishing a prima facie case of obviousness under 35 U.S.C. §103(a). *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). The Supreme Court in *KSR* emphasized that consideration of prior art that teaches away from the claimed invention is also relevant to the determination of obviousness. The Court stated that "when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007) (citing *United States v. Adams*, 383 U.S. 39, 40).

Finally, as recognized by the Office in the MPEP §2143.01, "[i]f [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." The Federal Circuit stated a similar principle in *In re Gordon*, indicating that where the proposed modification would render the prior art invention unsatisfactory for its intended purpose, the prior art invention effectively teaches away from the proposed modification. *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984)

Claim 71, the sole independent claim, recites:

A method for delivering a therapeutic agent into the inner ear of a living subject, said method comprising:

providing a drug delivery unit comprising a carrier material and a therapeutic agent combined therewith, wherein said carrier material provides for controlled release of the therapeutic agent from said drug delivery unit over time, and further wherein

said drug delivery unit is configured as a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, or strand, and

said drug delivery unit is shaped and sized for partial or complete insertion into the round window niche of the subject; and

inserting said drug delivery unit directly into the round window niche of the subject such that said unit is positioned either partially or completely within the round window niche, wherein the therapeutic agent is released from the drug delivery unit, contacts the round window membrane and passes into the inner ear.

The Office admits that Manning does not teach that the drug delivery unit is configured as one of the recited shapes in claim 71. Office Action, pg. 3, lines 13-16. In an attempt to remedy this deficiency in the primary reference, the Office proposes a combination of the teachings of Manning with the teachings of Tamada and Husmann.

Manning teaches away from the proposed combination

Manning teaches away from a drug delivery unit having a structure as set forth in the instant claims, i.e., a drug delivery unit ***"configured as a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, or strand"***. This is because Manning teaches a composition lacking a structure such that "**[t]he composition is fluid enough to be injected through a fine gauge needle (as small as 26 gauge).**" Manning at page 5, lines 24-25. See, also, Manning at page 10, lines 21-23, indicating that **"[t]he composition is always somewhat fluid, unlike solid implants or microspheres or other controlled release dosage forms**." This disclosure of Manning directs a person of ordinary skill in the art away from a drug delivery unit having a defined structure, such as those set forth in claim 71, in favor of a

composition of such fluidity that the composition may be injected through a fine gauge needle. Manning teaches that such fluidity assures proper placement of the composition. See, Manning at page 5, line 25.

For the reasons discussed above, Manning teaches away from the proposed combination with Tamada and Husmann. According to the Office, Tamada teaches drug delivery units configured as a solid disk, pellet, tablet or plate. Office Action, pg. 3, lines 19-21. According to the Office, Husmann teaches delivery of solid pieces of Gelfoam to the round window niche. Office Action, pg. 4, lines 21-22. Because Manning teaches the use of drug delivery units lacking a defined structure in order to achieve the goal of providing a fluid composition that may be injected through a fine gauge needle, one of ordinary skill in the art would have been directed away from references teaching the use of drug delivery units having a defined structure, such as those described in Tamada and Husmann.

The Office argues that "Manning only teaches away for solid drug delivery units made of hyaluronic acid but does not teach away for all solid drug delivery units." Office Action, pg. 4, lines 14-16. Applicants respectfully disagree. Manning identifies hyaluronic acid as a preferred polymeric component and indicates that other biocompatible polymers include those having characteristics similar to hyaluronic acid may be used. See, e.g., pg. 6, lines 24-30 of Manning. Accordingly, one of ordinary skill in the art reading the Manning reference would understand that composition characteristics indicated as suitable for hyaluronic acid compositions, i.e., those lacking a defined structure, would be suitable for compositions including polymers having similar characteristics. Likewise, composition characteristics indicated as unsuitable for hyaluronic acid compositions, i.e., those having a defined structure, would reasonably be considered unsuitable for compositions including polymers having similar characteristics to hyaluronic acid.

In addition, Manning states as a general goal of its disclosure the "[d]evelopment of a dosage form which could reliably deliver a fixed dose and remain in contact with the round membrane . . . ." Manning, pg. 3, lines 26-27. This goal is then addressed by Manning by indicating that "[t]he composition is fluid enough to be injected through a fine gauge needle (as small as 26 gauge), assuring proper placement of the gel, but viscous enough that it will remain in contact with the tissue for an extended period of time." Manning, pg. 5, lines 24-26. While the above goal is addressed in the context of a hyaluronic acid embodiment, one of ordinary skill in the art would understand this teaching to apply

more generally, i.e., that Manning directs one of ordinary skill in the art towards a composition fluid enough to be injected through a fine gauge needle and away from a composition having a defined structure such as those set forth in the instant claims.

According to the Office, "Tamada teaches solid drug delivery units with excellent drug delivery profiles and therefore the ordinary skilled artisan would not be deterred from using such a unit." However, one of ordinary skill in the art would have been deterred from using such a unit in the context of the method described in Manning because Manning teaches away from such embodiments for its specific method of delivery as discussed above.

Finally, Applicants note that the Office explicitly recites as alleged support those sections of Manning which discuss the use of hyaluronic acid. See, e.g., Office Action, pg. 3, lines 13-14, citing pg. 5, lines 24-26, of Manning. The Office cannot reasonably rely on these sections as alleged support for the claim elements without also considering those portions of Manning which discuss the use of hyaluronic acid and which teach away from the claim elements.

The Office proposes a modification of the composition of Manning which would result in Manning's fluid composition having one or more of the structures set forth in claim 71. However, Applicants submit that such a modification would render the composition of Manning **unsatisfactory for its intended purpose** because it would no longer be "fluid enough to be injected through a fine gauge needle" and accordingly Manning's goal of assuring proper placement via injection of a fluid composition would be thwarted. Thus, in accordance with the law as set forth in *In re Gordon*, **Manning effectively teaches away from the proposed modification**.

As discussed above, Manning explicitly directs a person of ordinary skill in the art away from a drug delivery unit having a defined structure, such as those set forth in claim 71. In addition, the Office's proposed modification of Manning which would result in Manning's fluid composition having one or more of the structures set forth in claim 71, would render the composition of Manning unsatisfactory for its intended purpose because it would no longer be "fluid enough to be injected through a fine gauge needle" and accordingly Manning teaches away from such a modification.

The Proposed Combination Fails to Disclose or Render Obvious All Elements of the Claims

With specific reference to claim 70, Applicants note that the Office has failed to demonstrate that the proposed combination of references discloses or renders obvious a method as claimed in claim 71, which includes the additional limitation of claim 70, "***wherein release of the therapeutic agent from the drug delivery unit is without inadvertent delivery to other tissue regions outside the round window niche***." Manning discloses injection or pumping of a fluid dosage form "behind the ear drum" to the middle ear. Manning, pg. 5, lines 20-21. If anything, this teaching of Manning suggests that inadvertent delivery to tissue regions outside the round window niche would be likely because of the fluid nature of the dosage form. Applicants note that while Husmann discusses placement of gentamicin "in the middle ear directly on the membrane covering the round window," (pg. 110, col. 2, last paragraph), this does not disclose or render obvious a method wherein release of the therapeutic agent from the drug delivery unit is without inadvertent delivery to other tissue regions outside the round window niche.

With specific reference to claims 83 and 85, Applicants note that the Office has failed to demonstrate that the proposed combination discloses or renders obvious a method as claimed in claim 71, which includes the additional limitation of claim 83 ***"wherein said drug delivery unit is shaped and sized for complete insertion into the round window niche of the subject***" or claim 85 ***"wherein said drug delivery unit is shaped and sized for complete insertion as a detached unit into the round window niche of the subject"***. At most, Manning discloses insertion into the middle ear such that the composition contacts the round window membrane and Husmann discloses placement on the round window membrane. However, neither Manning, Husmann, nor the combination thereof discloses or renders obvious a composition that is shaped and sized for complete insertion into the round window niche of the subject.

With specific reference to claim 86, Applicants note that the Office has failed to demonstrate that the proposed combination discloses or renders obvious a method as claimed in claim 71, which includes the additional limitation of claim 86 ***"wherein said drug delivery unit is positioned at a location which is spaced apart from the round window membrane."*** If anything, Manning teaches the opposite configuration. Manning explicitly teaches that its composition is in contact with the round window membrane. See, e.g., Manning at page 3, lines 26-29; and page 4, lines 10-14.

In view of the above, Applicants submit that the Office has failed to establish a *prima facie* case of obviousness under 35 U.S.C. §103(a). Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for the Request for Continued Examination and extensions of time, or credit any overpayment to Deposit Account No. 50-0185, order number DURE-021.

Respectfully submitted,
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